Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (Withdrawn) An isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of:

(a) a genomic nucleotide sequence encoding an ATP-gated ion channel P2X7R and which contains a mutation in the 5'UTR region corresponding to positions 362, 532, 1100, 1122, 1171 or 1702 of the genomic sequence of the wild-type ATP-gated ion channel P2X7R as depicted in SEQ ID NO: 1, wherein at said position said nucleotide is replaced by another nucleotide;

(b) a nucleic acid sequence encoding a polypeptide which has an amino acid sequence of the ATP-gated ion channel P2X7R, wherein in the exon as indicated in column "Exon" of the following Table A the amino acid residue as indicated in column "Amino acid residue" of Table A corresponding to the position as indicated in column "Position in wild-type" of Table A of the wild-type ATP-gated ion channel P2X7R amino acid sequence as depicted in SEQ ID NO: 3 or 4 is replaced by another amino acid residue

Table A

Exon	Amino acid residue	Position in wild-type
exon 3	R (Arg)	117
exon 5	G (Gly)	150
exon 6	E (Glu)	186
exon 6	L (Leu)	191
exon 8	R (Arg)	270
exon 13	I (Ile)	568
exon 13	R (Arg)	578

(c) a nucleotide sequence encoding an ATP-gated ion channel P2X7R and which contains a mutation in exon 5 or 8 corresponding to position 32548 or position 37633 of the wild-type ATP-gated ion channel P2X7R nucleotide sequence as depicted in

SEQ ID NO: 1, wherein at said position said nucleotide is replaced by another nucleotide

(d) a nucleic acid sequence encoding a polypeptide which has an amino acid sequence of an ATP-gated ion channel P2X7R, wherein amino acids corresponding to positions 488 to 494 of the wild-type ATP-gated ion channel P2X7R as depicted in SEQ ID NO: 3 or 4 are deleted;

(e) a genomic nucleotide sequence encoding an ATP-gated ion channel P2X7R, wherein in the intron as indicated in column "Intron" of the following Table B the nucleotide as indicated in column "Replaced nucleotide" of Table B corresponding to the position as indicated in column "Position in wild-type" of Table B of the wild-type ATP-gated ion channel P2X7R nucleotide sequence as depicted in SEQ ID NO: 1 is replaced by another nucleotide

Table B

Intron	REPLACED NUCLEOTIDE	**Position in wild-type**
intron 1	G	3166
intron 1	C	24778
intron 1	C	24830
intron 3	A	26308
intron 3	G	26422
intron 4	G	32394
intron 4	T	32434
intron 5	A	32783
intron 6	G	35641
intron 6	A	35725
intron 6	T	36001
intron 7	G	36378
intron 7	T	36387
intron 7	G	36398
intron 9	C	47214
intron 11	T	47563
intron 12	C	54307
intron 12	G	54308

(f) a genomic nucleotide sequence encoding an ATP-gated ion channel P2X7R and which contains a mutation in the 3'UTR region corresponding to position 54925, 55169, 55170, 55171 or 55917 of the wild-type ATP-gated ion channel P2X7R

nucleotide sequence as depicted in SEQ ID NO: 1, wherein at said position said nucleotide is replaced by another nucleotide;

(g) a nucleotide sequence comprising at least 20 or 21 nucleotides and comprising the mutations or deletions as defined in any one of (a) to (f);

(h) a nucleic acid sequence comprising a nucleotide sequence as shown in any one of SEQ ID NOs: 13 to 51;

(i) a nucleic acid sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NOs: 5 to 12;

(j) a nucleotide sequence which hybridizes to a nucleotide sequence defined in any one of (a) to (g) or to the nucleotide sequence of (h) and having a mutation as defined in any one of (a) to (f); and

(k) a nucleic acid sequence being degenerate as a result of the genetic code to the nucleic acid sequence as defined in (j).

2. (Withdrawn) The nucleic acid molecule of claim 1 derived from mouse, rat or human.

3. (Withdrawn) The nucleic acid molecule of claim 1 which is DNA, RNA, PNA or phosphorothioates.

4. (Withdrawn) A vector comprising the nucleic acid molecule of claim 1.

5. (Withdrawn) The vector of claim 4 which is an expression vector, a gene targeting vector and/or a gene transfer vector.

6. (Withdrawn) A host transformed with the nucleic acid molecule of claim 1 or a vector comprising said nucleic acid molecule.

7. (Withdrawn) The host of claim 6 which is a mammalian cell, an amphibian cell, a fish, an insect cell, a fungal cell, a plant cell or a bacterial cell.

8. (Withdrawn) The host of claim 7, wherein said mammalian cell is selected from the group consisting of CHO cells, HEK293 cells, COS-7 cells or PC12 cells.

9. (Withdrawn) The host of claim 7, wherein said amphibian cell is an oocyte, preferably a Xenopus oocyte.

10. (Withdrawn) The host of claim 9, wherein said oocyte is a frog oocyte.

11. (Withdrawn) The host of claim 6 which is a non-human transgenic organism.

12. (Withdrawn) The host of claim 11, wherein said non-human organism is a mammal, amphibian, a fish, an insect, a fungus or a plant.

13. (Withdrawn) A method for producing the polypeptide encoded by a nucleic acid molecule of claim 1(b) or 1(d) comprising culturing/raising a host transformed with the nucleic acid molecule of claim 1 or a vector comprising said nucleic acid molecule and isolating the produced polypeptide.

14. (Withdrawn) A polypeptide encoded by the nucleic acid molecule of claim 1(b) or 1(d) or produced by a method comprising culturing/raising a host transformed with the nucleic acid molecule of claim 1 or a vector comprising said nucleic acid molecule.

15. (Withdrawn) An antibody specifically directed to the polypeptide of claim 14, wherein said antibody specifically reacts with an epitope generated and/or formed by the mutation in the ATP-gated ion channel P2X7R selected from the group consisting of:
(i) an epitope specifically presented by a polypeptide which has an amino acid sequence of an ATP-gated ion channel P2X7R, wherein the R (Arg), G (Gly), E (Glu), L (Leu), R (Arg), I (Ile) or R (Arg) residue corresponding to position 117, 150, 186, 191, 270, 568 or 578 of the wild-type ATP-gated ion channel P2X7R as depicted in SEQ ID NO: 3 or 4 is replaced by another amino acid residue; and
(ii) an epitope specifically presented by a polypeptide which has an amino acid sequence of an ATP-gated ion channel P2X7R, wherein amino acids corresponding to positions 488 to 494 of the wild-type ATP-gated ion channel P2X7R as depicted in SEQ ID NO: 3 or 4 are deleted.

16. (Withdrawn) The antibody of claim 15 which is a monoclonal antibody.

17. (Withdrawn) An aptamer specifically binding to a nucleic acid molecule of claim 1 or to the polypeptide encoded by the nucleic acid molecule of claim 1.

18. (Withdrawn) A primer or pair of primers capable of specifically amplifying a nucleic acid molecule as defined in claim 1.

19. (Withdrawn) The primer or pair of primers of claim 18, which is selected from the group consisting of SEQ ID NOs.: 52 to 111.

20. (Withdrawn) A composition comprising the nucleic acid molecule of claim 1, a vector comprising said nucleic acid molecule, a polypeptide encoded by said nucleic acid molecule, an antibody specifically directed to said polypeptide, an aptamer specifically binding to said nucleic acid molecule and/or a primer or pair of primers capable of specifically amplifying said nucleic acid molecule.

21. (Withdrawn) The composition of claim 20 which is a diagnostic composition.

22. (Withdrawn) The composition of claim 21, optionally further comprising suitable means for detection.

23. (Cancelled).

24. (Withdrawn) A method of diagnosing an affective disorder or a susceptibility to an affective disorder comprising the step of determining in a sample obtained from an individual whether the P2XR7 protein expressed in the cells of said individual is non-functional, shows an altered ATP-gating in comparison to the wild-type P2XR7 protein or is over- or under-expressed in comparison to the P2XR7 protein level an unaffected individual.

25. (Withdrawn) A method for diagnosing an affective disorder or a susceptibility to an affective disorder comprising the step of determining in a sample obtained from an individual whether the P2X7R gene sequence or encoded protein thereof comprises a mutation in comparison to the wild-type P2X7R sequence.

26. (Withdrawn) A method for diagnosing an affective disorder or a susceptibility to an affective disorder comprising the step of determining in a sample obtained from an

individual whether the P2X7R gene sequence or encoded protein thereof comprises a mutation in comparison to the wild-type P2X7R sequence, wherein said mutation is a mutation as defined in claim 1 and/or a nucleotide replacement or deletion selected from the following Table C indicating in column "Region of P2X7R" the region of the P2X7R genomic nucleotide sequence in which the replacement or deletion occurs, in column "Nucleotide" of Table C the nucleotide which is replaced by another nucleotide or the nucleotides which are deleted and in column "Position in wild-type" of Table C the corresponding position in the nucleotide sequence of the wild-type ATP-gated ion channel P2X7R as depicted in SEQ ID NO: 1

Table C

Region of P2X7R	NUCLEOTIDE	**Position in wild-type**
5'UTR	T	362
5'UTR	T	532
5'UTR	A	1100
5'UTR	A	1122
5'UTR	C	1171
5'UTR	T	1351
5'UTR	G	1702
5'UTR	T	1731
5'UTR	C	1860
5'UTR	C	2162
5'UTR	C	2238
5'UTR	A	2373
5'UTR	G	2569
5'UTR	G	2702
intron 1	G	3166
intron 1	C	24778
intron 1	C	24830
exon 2	T	24942
exon 3	C	26188
exon 3	A	26308
exon 3	G	26422
intron 4	G	32394
intron 4	T	32434
exon 5	G	32493
exon 5	G	32506
exon 5	C	32507

exon 5	C	32548
intron 5	A	32783
intron 5	T	35309
intron 5	C	35374
intron 5	A	35378
exon 6	G	35438
exon 6	T	35454
intron 6	T	35549
intron 6	G	35641
intron 6	A	35725
intron 6	T	36001
intron 6	A	36064
intron 6	deletion of GTTT	36091 to 36094
intron 6	C	36108
intron 7	C	36374
intron 7	G	36378
intron 7	T	36387
intron 7	G	36398
intron 7	C	37439
intron 7	T	37513
exon 8	C	37604
exon 8	G	37605
exon 8	G	37623
exon 8	C	37633
intron 9	C	47214
exon 11	G	47383
exon 11	C	47411
intron 11	T	47563
intron 12	C	54307
intron 12	G	54308
exon 13	C	54399
exon 13	A	54480
exon 13	C	54523
exon 13	deletion of CCCTGAGAGCCACAGGTGCCT	54562 to 54582
exon 13	A	54588
exon 13	C	54664
exon 13	G	54703
exon 13	A	54804
exon 13	G	54834
exon 13	G	54847
3'UTR	G	54925
3'UTR	C	55169
3'UTR	A	55170

3'UTR	A	55171
3'UTR	C	55917

27. (Withdrawn) The method of claim 26, wherein the occurrence of the mutation in the ATP-gated ion channel P2X7R gene is determined by PCR or immunological methods.

28. (Withdrawn) The composition of claim 20 which is a pharmaceutical composition.

29. (Withdrawn) The pharmaceutical composition of claim 28, optionally further comprising a pharmaceutically acceptable carrier.

30. (Withdrawn) A method of treating an affective disorder comprising administering a therapeutically effective amount of the nucleic acid molecule as defined in claim 1 or a therapeutically effective amount of a polypeptide encoded by said nucleic acid molecule to a subject suffering from said disorder.

31. (Cancelled).

32. (Withdrawn) A pharmaceutical composition comprising a nucleic acid molecule comprising a nucleotide sequence which encodes a functional ATP-gated ion channel P2X7R and which is selected from the group consisting of:

(a) a nucleotide sequence encoding a polypeptide comprising the amino acid sequence as depicted in SEQ ID NO: 3 or 4;

(b) a nucleotide sequence comprising the nucleotide sequence as depicted in SEQ ID NO: 1 or 2;

(c) a nucleotide sequence which hybridizes to the nucleotide sequence of (a) or (b); and

(d) a nucleotide sequence which is degenerated as a result of the genetic code to the nucleotide sequence of (c).

33. (Withdrawn) A pharmaceutical composition comprising a compound the administration of which to cells leads to an increase of the expression of a nucleic acid encoding an ATP-gated ion channel P2X7R in the cells or comprising a nucleic acid molecule

the expression of which in cells or the administration of which to cells leads to an increase of the expression of a nucleic acid encoding an ATP-gated ion channel P2X7R in the cells.

34. (Withdrawn) A method of treating an affective disorder comprising administering a therapeutically effective amount of the pharmaceutical composition as defined in claim 32, a pharmaceutical composition comprising a compound the administration of which to cells leads to an increase of the expression of a nucleic acid encoding an ATP-gated ion channel P2X7R in the cells, a pharmaceutical composition comprising a nucleic acid molecule the expression of which in cells or the administration of which to cells leads to an increase of the expression of a nucleic acid encoding an ATP-gated ion channel P2X7R in the cells or a pharmaceutical composition comprising a polypeptide encoded by said nucleic acid molecule to a subject suffering from said disorder.

35. (Cancelled).

36. (Currently Amended) A method of treating ~~an affective disorder~~ **major depression** comprising administering a therapeutically effective amount of a pharmaceutical composition comprising ~~a modulator~~ **an agonist** of ATP-gated ion channel purinergic receptor P2X7 (P2X7R) activity to a subject suffering from said ~~affective disorder~~ **major depression**.

37. (Cancelled).

38. (Withdrawn and Currently Amended) The method of claim ~~37~~ **36**, wherein said agonist is selected from the group consisting of ATP, ATP-4 and BzATP (2'-3'-O-(4-Benzoylbenzoyl)adenosine 5'-triphosphate ($C_{24}H_{24}N_5O_{15}P_3$)).

39. (Currently Amended) The method of claim ~~37~~ **36**, wherein said agonist is tenidap ($C_{15}H_{11}ClN_2O_2S$) or a derivative thereof or 3-substituted-2-oxindole-1-carboxamides.

40. (Previously Presented) The method of claim 36, wherein said pharmaceutical composition optionally further comprises a β-adrenergic receptor modulator.

41. (Previously Presented) The method of claim 40, wherein said β-adrenergic receptor modulator is a β-adrenergic receptor antagonist selected from the group consisting of DL-propanolol, D-propanolol and labetolol.

42. (Cancelled).

43. (Currently Amended) The method of claim ~~42~~ **36**, wherein said major depression is selected from the group consisting of major depression, dysthymia, atypical depression, premenstrual dysphoric disorder and seasonal affective disorder.

44. (Cancelled)

45. (Cancelled)

46. (Withdrawn) A kit comprising the nucleic acid molecule of claim 1, a vector comprising said nucleic acid molecule, a host comprising said nucleic acid molecule, a polypeptide encoded by said nucleic acid molecule , an antibody specifically directed to said polypeptide, an aptamer specifically binding to said nucleic acid molecule and/or a primer or pair of primers capable of specifically amplifying said nucleic acid molecule.

47. (Withdrawn) A method for identifying compounds which are capable of specifically interacting with the polypeptide of claim 14, comprising the steps of

contacting a polypeptide of claim 14 with a compound or a candidate mixture of compounds to be tested; and

determining whether said compound or a candidate mixture of compounds is capable of specifically interacting with said polypeptide.

48. (Withdrawn) A method for the characterization of compounds which are capable of altering characteristics of the polypeptide of claim 14, comprising the steps of

contacting a polypeptide of claim 14 with a compound or a candidate mixture; and

determining whether the compound or a candidate mixture alters a characteristic of the polypeptide of claim 14.

49. (Withdrawn) A method of screening for compounds which are capable of interacting with the polypeptide of claim 14, comprising the steps of

(a) contacting a polypeptide of claim 14 with a compound or a candidate mixture of compounds;

(b) measuring and/or detecting a response; and

(c) comparing said response to a standard response as measured in the absence of said candidate molecule.

50. (Withdrawn) A method for the production of a pharmaceutical composition comprising the steps of the method of claim 47 and comprising a further step, wherein a derivative of said identified, characterized and/or screened molecule is generated.

51. (Withdrawn) A method for the production of a pharmaceutical composition comprising the steps of the method of claim 47 and formulating the molecules identified, characterized, screened and/or derivatized in pharmaceutically acceptable form.

52. (Withdrawn) The method of claim 51, wherein the pharmaceutical composition to be produced further comprises neuroprotective substances, nootrophic substances, brilliant blue, piperidine or piperazine derivatives thereof, adamantine derivatives, substituted phenyl compounds, oxidized ATP, 2-O-(4-benzoylbenzoyl)adenosine-5-triphosphate, 3-O-(4-benzoylbenzoyl)adenosine-5-triphosphate or β-adrenergic receptor modulators.

53. (Withdrawn) The method of claim 47, wherein said compound(s) or candidate mixture(s) of compounds comprise(s) antagonist(s), partial antagonist(s), partial agonist(s) and/or agonist(s) for an altered ATP-gated ion channel P2X7R.

54. (Withdrawn) A method for diagnosing an affective disorder of an individual comprising:

(a) isolating DNA from cells obtained from an individual;

(b) determining all or part of the nucleotide composition of the P2X7R gene; and

(c) analyzing said nucleotide composition of P2X7R for the presence of one or more polymorphism(s) mutation or allelic variation.

55. (Withdrawn) A method for diagnosing an affective disorder of an individual comprising:

(a) isolating RNA from cells obtained from an individual;

(b) converting said RNA into cDNA;

(c) determining all or part of the nucleotide composition of the P2X7R gene; and

(d) analyzing said nucleotide composition of P2X7R for the presence of one or more polymorphism(s), mutation or allelic variation.

56. (Withdrawn) A method for diagnosing an affective disorder of an individual comprising:

(a) isolating RNA or protein from cells obtained from an individual ;

(b) determining the levels of P2X7R RNA or protein; and

(c) comparing the levels of P2X7R RNA or protein with the corresponding levels from a normal individual not afflicted with an affective disorder.